

CLAIMS

1. A lung surfactant composition comprising a lung surfactant, which - when dispersed as powder or particles in 0.9% w/w sodium chloride in a concentration of 10% w/w at ambient temperature is capable of forming, in the course of swelling, a birefringent network or tubules at an air-liquid-solid interface within a time period of from about 0.5 min to about 120 minutes as observed by polarising microscopy.
2. A lung surfactant composition, which - when dispersed as a powder or as particles in an electrolyte solution having an ionic strength of at least about 5 mM or at an ionic strength corresponding to physiological conditions, and the thus obtained dispersion has a concentration of water of at least about 55% w/w, - is subject to a dynamic swelling process during which a birefringent network or tubules are formed, as observed by polarising microscopy, and the dynamic swelling process ends when steady-state is reached.
3. A lung surfactant composition according to claim 2, wherein the electrolyte solution has an ionic strength of at least about 10 mM such as, e.g., at least about 15 mM, at least about 20 mM, at least about 25 mM, at least about 50 mM, at least about 75 mM, at least about 100 mM or at least about 125 mM.
4. A lung surfactant composition according to claim 2, wherein the dispersion obtained has a concentration of water of at least about 60% such as, e.g., at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or at least about 98% w/w.
5. A lung surfactant composition according to claim 2, wherein the lung surfactant - when dispersed in an electrolyte solution - is in the form of a liquid crystalline lamellar phase.
6. A lung surfactant composition according to claim 2, wherein the electrolyte solution comprises at least one of the following cationic species: Na^+ , K^+ , Li^+ , Ca^{2+} , Mg^{2+} and/or NH_4^+ .
7. A lung surfactant composition according to claim 2, wherein the electrolyte solution comprises at least one of the following anionic species: chloride, acetate, carbonate,

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hydrogen carbonate, dihydrogen phosphate (H_2PO_4^-), monohydrogen phosphate (HPO_4^{2-}), phosphate (PO_4^{3-}), tartrate, citrate, borate, fumarate, or the like.

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- 5 8. A lung surfactant composition according to claim 2, wherein the electrolyte solution is a sodium chloride solution such as, e.g. a 0.9% w/w sodium chloride solution, Ringer solution or Ringer-acetate solution.
- 10 9. A lung surfactant composition according to claim 1 or 2, wherein the lung surfactant comprises phospholipids.
- 10 10. A lung surfactant composition according to claim 1 or 2, wherein the lung surfactant comprises phospholipids, which are present in the form of a mixture of saturated and unsaturated phospholipids.
- 112 15 11. A lung surfactant composition according to claim 9, wherein the concentration of phospholipids is from about 80 to about 99.5% w/w such as, e.g. from about 85 to about 98% w/w or from about 90 to about 98% w/w of the composition in dry form.
- 20 12. A lung surfactant composition according to claim 1 or 2 comprising dipalmitylphosphatidylcholine (DPPC).
- 112 25 13. A lung surfactant composition according to claim 1 or 2 comprising surfactant proteins such as, e.g., SP-A, SP-B, SP-C and/or SP-D. *object*
- 30 14. A lung surfactant composition according to claim 13, wherein the surfactant proteins are SP-B and/or SP-C.
- 112 35 15. A lung surfactant composition according to claim 13, wherein the total concentration of surfactant proteins is from about 0.5 to about 10% w/w such as, e.g., from about 0.5% to about 7.5% w/w, from about 0.5 to about 5% w/w, from about 0.5 to about 2.5% w/w or from about 0.5% to about 2% w/w of the composition in dry form.
16. A lung surfactant composition according to claim 1 or 2 comprising at the most up to 10% w/w of other lipids than phospholipids.
17. A lung surfactant composition according to claim 1 or 2, wherein the lung surfactant is obtained from a mammalian lung.

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18. A lung surfactant composition according to claim 17, wherein the lung surfactant is extracted from the mammalian lung.
- 5 19. A lung surfactant composition according to claim 17, wherein the mammalian lung is cattle, bovine, porcine, monkey or human lung.
- 10 20. A lung surfactant composition according to claim 1 or 2, wherein the lung surfactant is obtained synthetically or semi-synthetically.
21. A lung surfactant composition according to claim 1 or 2, wherein the lung surfactant is obtained from mammalian alveolar cell cultures.
- 15 22. A lung surfactant composition according to claim 13, wherein the surfactant protein is a recombinant protein.
23. A lung surfactant composition according to claim 1 or 2 further comprising one or more inorganic or organic salts, which impart ionic strength to the composition when dispersed in an aqueous medium such as, e.g., water.
- 20 24. A lung surfactant composition according to claim 23, wherein the inorganic salts are selected from the group consisting of alkaline metal salt such as, e.g., sodium chloride, potassium chloride, lithium chloride and alkaline earth metal salts such as, e.g. calcium chloride, magnesium chloride etc.
- 25 25. A lung surfactant composition according to claim 23, wherein the organic salts are selected from the group consisting of acetates such as, e.g., sodium-acetate, potassium acetate, lithium acetate, citrates, tartrates, fumarates, borates, phosphates, ammonium salt such as e.g. ammonium chloride etc.
- 30 26. A lung surfactant composition according to claim 1 or 2 further comprising another therapeutically, prophylactically and/or diagnostically active substance.
- 35 27. A method for treating and/or preventing infant respiratory distress syndrome (IRDS), adult respiratory distress syndrome (ARDS), congenital diaphragmatic hernia, acute lung injury, patients treated with Extracorporeal Membrane Oxygenation and/or meconium aspiration pneumonia, the method comprising administering to a mammal,

Including a human, in need thereof a sufficient amount of a lung surfactant composition according to any of claims 1-26.

28. A method for treating and/or preventing chronic obstructive lung disease, asthma, acute bronchitis, chronic bronchitis, bronchopulmonary dysplasia, lung infections, persistent pulmonary hypertension, lung hypoplasia, cancer, cystic fibrosis, alveolar proteinosis and/or congenital SP-B deficiency, the method comprising administering to a mammal, including a human, in need thereof a sufficient amount of a lung surfactant composition according to any of claims 1-26.
29. A method according to claim 27 or 28, wherein the lung surfactant composition is administered as a medicament prepared by dispersing the lung surfactant in powder or particulate form in a suitable dispersion medium.
30. A method according to claim 29, wherein dispersing is performed for a sufficient period of time to ensure dynamic swelling and formation of a birefringent network or tubules.
31. A method according to claim 30, wherein the sufficient period of time is from about 0.5 to about 120 min such as, e.g., from about 1 to about 100 min, from about 2 to about 90 min, from about 2 to about 80 min, from about 2 to about 70 min, from about 3 to about 60 min, from about 3 to about 50 min, from about 3 to about 45 min, from about 5 to about 40 min, from about 5 to about 35 min, from about 10 to about 35 min, from about 15 to about 35 min or from about 20 to about 35 min.
32. A pharmaceutical composition comprising a lung surfactant composition according to any of claims 1-26.
33. A pharmaceutical composition according to claim 32 in powder or particulate form adapted to be dispersed in an aqueous medium before use.
34. A pharmaceutical composition according to claim 32 in liquid form.
35. A pharmaceutical composition according to claim 34, wherein the liquid is in the form of a dispersion comprising the lung surfactant composition and an electrolyte solution.
36. A pharmaceutical composition according to claim 32, wherein the composition is adapted to physiological conditions.

37. A pharmaceutical composition according to claim 35, wherein the electrolyte solution is a physiologically acceptable solution.

5 38. A pharmaceutical composition according to claim 32 further comprising another therapeutically, prophylactically and/or diagnostically active substance.

39. A pharmaceutical composition according to claim 32 in the form of a powder or particles adapted to be administered from an inhaler or the like.

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40. A pharmaceutical composition according to claims 39, wherein the mean particle size and/or the electrostatic properties of the powder or particles have been adjusted to conditions required in order to reach specific sites in the respiratory organs after administration via an inhaler or the like.

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41. A pharmaceutical kit comprising a first and a second container, the first container comprising a lung surfactant composition according to any of claims 1-26 and the second container comprising a dispersion medium for the lung surfactant composition, accompanied by instructions for dispersing the lung surfactant composition in the dispersion medium before use.

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42. A pharmaceutical kit according to claim 41, wherein the lung surfactant composition is in powder or particulate form.

25 43. A pharmaceutical kit according to claim 41, wherein the instructions include recommendations for the time period during which the lung surfactant composition should be administered after dispersion in the dispersion medium.

30 44. A pharmaceutical kit according to claim 41, wherein the dispersion medium is an electrolyte solution.

45. A pharmaceutical kit according to claim 44, wherein the electrolyte solution is a physiologically acceptable electrolyte solution such as, e.g. 0.9% w/w sodium chloride solution, Ringer solution or Ringer-acetate solution.

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46. A pharmaceutical kit according to claim 41 further comprising another therapeutically, prophylactically and/or diagnostically active substance.

47. A pharmaceutical kit comprising a first and a second container, the first container being in the form of an inhaler or the like comprising a pharmaceutical composition according to claims 39 or 40, and the second container being in the form of a nebuliser or the like comprising an appropriate medium, which – when administered after administration of the pharmaceutical composition of the first container – ensures formation of a suitable *in situ* microenvironment for a dynamic swelling process.
48. A method for the treatment and/or prevention of a lung disease or condition in a mammal, the method comprising administering to the mammal in need thereof an effective amount of a lung surfactant composition according to any of claims 1-26.
49. A method according to claim 48, wherein the lung surfactant composition is administered in the form of a pharmaceutical composition according to any of claims 32-40.
50. A method according to claim 48 or 49, wherein the administration takes place during a dynamic swelling phase of the lung surfactant composition.
51. A method according to claim 48, wherein the lung disease or condition is selected from the group consisting of Infant respiratory distress syndrome (IRDS), adult respiratory distress syndrome (ARDS), congenital diaphragmatic hernia, acute lung injury, patients treated with Extracorporeal Membrane Oxygenation and meconium aspiration pneumonia.
52. A method according to claim 48, wherein the lung disease or condition is selected from the group consisting of chronic obstructive lung disease, asthma, acute bronchitis, chronic bronchitis, bronchopulmonary dysplasia, lung infections, persistent pulmonary hypertension, lung hypoplasia, cancer, cystic fibrosis, alveolar proteinosis and congenital SP-B deficiency.
53. A method for the preparation of a pharmaceutical composition, the preparation comprising dispersing a lung surfactant composition according to any of claims 1-26 in an electrolyte solution having an ionic strength of at least about 5 mM so as to enable a dynamic swelling of the lung surfactant within a time period of from about 0.5 to about 120 min, and the dynamic swelling is observed by polarisation microscopy as a birefringent network or tubules formed at an air-liquid-solid interface.

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- a) determining $t_{\frac{1}{2}}$ for maximum dynamic swelling as described herein,
- b) comparing the thus obtained $t_{\frac{1}{2}}$ with a *in vivo* – *in vitro* correlation curve, obtained as described herein, and

c) evaluating the batch as acceptable or not acceptable.

- 5 ~~62.~~ An *in vitro* method for evaluating the therapeutic, prophylactic and/or diagnostic effect of a lung surfactant composition, which has dynamic swelling behaviour when dispersed in an electrolyte solution, the method comprising determining the half-life of the steady-state swelling and comparing the thus obtained half-life with *in vivo-in vitro* correlation curves in order to predict the therapeutic, prophylactic and/or diagnostic effect.

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